CLAIMS

We claim:

1. A method, comprising:

a) providing:

i) a folded target having a deoxyribonucleic acid sequence comprising one or more double stranded regions and one or more single stranded regions; and

ii) one or more oligonucleotide probes complementary to at least a portion of said folded target; and

b) mixing said folded target and said one or more probes under conditions such that said probe hybridizes to said folded target to form a probe/folded target complex.

2. The method of Claim 1, further comprising detecting the presence of said probe/folded target complex.

3. The method of Claim 1, further comprising quantitating the amount of probe/folded target complex formed.

4. The method of Claim 1, wherein said probe in said probe/folded target complex is hybridized to a single stranded region of said folded target.

5. The method of Claim 2, wherein said probe comprises an oligonucleotide having a moiety that permits its capture by a solid support.

6. The method of Claim 5, wherein said detecting the presence of said probe/folded target complex comprises exposing said probe/folded target complex to a solid support under conditions such that said probe is captured by said solid support.

7. The method of Claim 6, wherein said moiety comprises a biotin moiety and said solid support comprises a surface having a compound capable of binding to said biotin moiety, said compound selected from the group consisting of avidin and streptavidin.

8. The method of Claim 1, wherein said folded target is labelled.

9. The method of Claim 2, wherein said folded target comprises a deoxyribonucleic acid sequence having a moiety that permits its capture by a solid support.

10. The method of Claim 9, wherein said detecting the presence of said probe/folded target complex comprises exposing said probe/folded target complex to a solid support under conditions such that said folded target is captured by said solid support.

11. The method of Claim 10, wherein said moiety comprises a biotin moiety and said solid support comprises a surface having a compound capable of binding to said biotin moiety, said compound selected from the group consisting of avidin and streptavidin.

12. The method of Claim 1, wherein said probe is labelled.

13. The method of Claim 1, wherein said probe is attached to a solid support.

14. The method of Claim 1, wherein said folded target nucleic acid is attached to a solid support.

15. A method, comprising:

a) providing:

i) a first folded target having a nucleic acid sequence comprising first and second portions, said first and second portions each comprising one or more double stranded regions and one or more single stranded regions;

ii) a second folded target having a nucleic acid sequence comprising a first portion that is identical to said first portion of said first folded target and a second portion that differs from said second portion of said first folded target because of a variation in nucleic acid sequence relative to said first folded target, said first and second portions each comprising one or more double stranded regions and one or more single stranded regions;

iii) first and second oligonucleotide probes, said first oligonucleotide probe complementary to said first portion of said first and second folded targets and said second oligonucleotide probe complementary to said second portion of said first and second folded targets; and

iv) a solid support comprising first, second, third and fourth testing zones, each zone capable of capturing and immobilizing said first and second oligonucleotide probes;

b) contacting said first folded target with said first oligonucleotide probe under conditions such that said first probe binds to said first folded target to form a probe/folded target complex in a first mixture;

c) contacting said first folded target with said second oligonucleotide probes under conditions such that said second probe binds to said first folded target to form a probe/folded target complex in a second mixture;

d) contacting said second folded target with said first oligonucleotide probe to form a third mixture;

e) contacting said second folded target with said second oligonucleotide probe to form fourth mixture; and

f) adding said first, second, third and fourth mixtures to said first, second, third and fourth testing zones of said solid support, respectively, under conditions such that said probes are captured and immobilized.

16. The method of Claim 15, wherein said first probe in step d) does not substantially hybridize to said second folded target.

17. The method of Claim 15, wherein the hybridization of said first probe in step d) to said second folded target is reduced relative to the hybridization of said first probe in step c) to said first folded target.

18. The method of Claim 15, wherein said first and second targets comprise DNA.

19. The method of Claim 15, wherein said first and second oligonucleotide probes comprise DNA.

20. A method, comprising:

a) providing:

i) a first folded target having a nucleic acid sequence comprising first and second portions, said first and second portions each comprising one or more double stranded regions and one or more single stranded regions;

ii) a second folded target having a nucleic acid sequence comprising a first portion that is identical to said first portion of said first folded target and a second portion that differs from said second portion of said first folded target because of a variation in nucleic acid sequence relative to said first folded target, said first and second portions each comprising one or more double stranded regions and one or more single stranded regions;

iii) a solid support comprising first and second testing zones, each of said zones comprising immobilized first and second oligonucleotide probes, said first oligonucleotide probe complementary to said first portion of said

first and second folded targets and second oligonucleotide probe complementary to said second portion of said first and second folded targets; and

b) contacting said first and second folded targets with said solid support under conditions such that said first and second probes hybridize to said first folded target to form a probe/folded target complex.

21. The method of Claim 20, wherein said contacting of step b) comprises adding said first folded target to said first testing zone and adding said second folded target to said second testing zone.

22. The method of Claim 21, wherein said first and second probes are immobilized in separate portions of said testing zones.

23. The method of Claim 22, wherein said first probe in said second testing zone does not substantially hybridize to said second folded target.

24. The method of Claim 22, wherein said first probe in said second testing zone hybridizes to said second folded target with a reduced efficiency compared to the hybridization of said first probe in first testing zone to said first folded target.

25. The method of Claim 20, wherein said first and second folded targets comprise DNA.

26. The method of Claim 20, wherein said first and second folded targets comprise RNA.

27. The method of Claim 20, wherein said first and second oligonucleotide probes comprise DNA.

28. A method for determination of structure formation in nucleic acid targets, comprising the steps of:

a) providing:

i) a folded target having a deoxyribonucleic acid sequence comprising one or more double stranded regions, and one or more single stranded regions, and further comprising two or more non-contiguous portions, and one or more intervening regions; and

ii) one or more bridging oligonucleotide probes complementary to said two or more non-contiguous portions of said folded target; and

b) mixing said folded target and said one or more probes under conditions such that said probe hybridizes to said folded target to form a probe/folded target complex.

29. The method of Claim 28, wherein said one or more intervening regions of said folded target comprises at least five nucleotides.

30. The method of Claim 28, further comprising detecting the presence of said probe/folded target complex.

31. The method of Claim 28, further comprising quantitating the amount of probe/folded target complex formed.

32. The method of Claim 28, wherein said probe in said probe/folded target complex is hybridized to at least one single stranded region of said folded target.

33. The method of Claim 30, wherein said bridging oligonucleotide probe further comprises a moiety that permits the capture of said bridging oligonucleotide probe by a solid support.

34. The method of Claim 33, wherein said detecting the presence of said probe/folded target complex comprises exposing said probe/folded target complex to a solid support under conditions such that said bridging oligonucleotide is captured by said solid support.

35. The method of Claim 34, wherein said moiety comprises a biotin moiety and said solid support comprises a surface having a compound capable of binding to said biotin moiety, said compound selected from the group consisting of avidin and streptavidin.

36. The method of Claim 28, wherein said folded target is labelled.

37. The method of Claim 30, wherein said folded target comprises a deoxyribonucleic acid sequence having a moiety that permits its capture by a solid support.

38. The method of Claim 37, wherein said detecting the presence of said probe/folded target complex comprises exposing said probe/folded target complex to a solid support under conditions such that said folded target is captured by said solid support.

39. The method of Claim 38, wherein said moiety comprises a biotin moiety and said solid support comprises a surface having a compound capable of binding to said biotin moiety, said compound selected from the group consisting of avidin and streptavidin.

40. The method of Claim 28, wherein said bridging oligonucleotide probe is labelled.

41. The method of Claim 28, wherein said bridging oligonucleotide probe is attached to a solid support.

42. The method of Claim 28, wherein said folded target nucleic acid is attached to a solid support.

43. A method for analyzing the structure of nucleic acid targets, comprising:

a) providing:

i) a first folded target having a nucleic acid sequence comprising first and second portions, said first and second portions each comprising one or more double stranded regions, and one or more single stranded regions, and further comprising two or more non-contiguous portions, and one or more intervening regions;

ii) a second folded target having a nucleic acid sequence comprising a first portion that is identical to said first portion of said first folded target and a second portion that differs from said second portion of said first folded target because of a variation in nucleic acid sequence relative to said first folded target, said first and second portions each comprising one or more double stranded regions, and one or more single stranded regions, and further comprising two or more non-contiguous portions, and one or more intervening regions;

iii) first and second bridging oligonucleotides, said first bridging oligonucleotide complementary to said two or more non-contiguous portions of said first portion of said first and second folded targets and said second bridging

oligonucleotide complementary to said two or more non-contiguous portions of said second portion of said first and second folded targets; and

iv) a solid support comprising first, second, third and fourth testing zones, each zone capable of capturing and immobilizing said first and second bridging oligonucleotides;

b) contacting said first folded target with said first bridging oligonucleotide under conditions such that said first bridging oligonucleotide binds to said first folded target to form a probe/folded target complex in a first mixture;

c) contacting said first folded target with said second bridging oligonucleotide under conditions such that said second bridging oligonucleotide binds to said first folded target to form a probe/folded target complex in a second mixture;

d) contacting said second folded target with said first bridging oligonucleotide to form a third mixture;

e) contacting said second folded target with said second bridging oligonucleotide to form fourth mixture; and

f) adding said first, second, third and fourth mixtures to said first, second, third and fourth testing zones of said solid support, respectively, under conditions such that said first and second bridging oligonucleotides are captured and immobilized.

44. The method of Claim 43, wherein said first bridging oligonucleotide in step d) does not substantially hybridize to said second folded target.

45. The method of Claim 43, wherein the hybridization of said first bridging oligonucleotide in step d) to said second folded target is reduced relative to the hybridization of said first bridging oligonucleotide in step c) to said first folded target.

46. The method of Claim 43, wherein said first and second targets comprise DNA.

47. The method of Claim 43, wherein said first and second bridging oligonucleotides comprise DNA.

48. A method for analyzing folded nucleic acid targets, comprising:

a) providing:

i) a first folded target having a nucleic acid sequence comprising first and second portions, wherein said first and second portions each comprise one or more double stranded regions and one or more single stranded regions;

ii) a second folded target having a nucleic acid sequence comprising a first portion that is identical to said first portion of said first folded target, and a second portion that differs from said second portion of said first folded target because of a variation in nucleic acid sequence relative to said first folded target, said first and second portions each comprising one or more double stranded regions and one or more single stranded regions;

iii) a solid support comprising first and second testing zones, each of said zones comprising immobilized first and second bridging oligonucleotides, said first bridging oligonucleotide complementary to said first portion of said first and second folded targets and second bridging oligonucleotide complementary to said second portion of said first and second folded targets; and

b) contacting said first and second folded targets with said solid support under conditions such that said first and second bridging oligonucleotides hybridize to said first folded target to form a probe/folded target complex.

49. The method of Claim 48, wherein said contacting of step b) comprises adding said first folded target to said first testing zone and adding said second folded target to said second testing zone.

50. The method of Claim 48, wherein said first and second bridging oligonucleotides are immobilized in separate portions of said testing zones.

51. The method of Claim 50, wherein said first bridging oligonucleotide in said second testing zone does not substantially hybridize to said second folded target.

52. The method of Claim 50, wherein said first bridging oligonucleotide in said second testing zone hybridizes to said second folded target with a reduced efficiency compared to the hybridization of said first bridging oligonucleotide in first testing zone to said first folded target.

53. The method of Claim 48, wherein said first and second folded targets comprise DNA.

54. The method of Claim 48, wherein said first and second folded targets comprise RNA.

55. The method of Claim 48, wherein said first and second bridging oligonucleotides comprise DNA.

56. A method, comprising:

a) providing:

i) target nucleic acid comprising first and second non-contiguous single-stranded regions separated by an intervening region comprising a double-stranded portion;

ii) a bridging oligonucleotide capable of binding to said first and second non-contiguous single-stranded regions; and

iii) a reactant selected from the group consisting of polymerases and ligases; and

b) mixing said target nucleic acid, said bridging oligonucleotide and said reactant under conditions such that said bridging oligonucleotide is modified to produce a modified oligonucleotide.

57. The method of Claim 56, wherein said reactant is a polymerase, and said modified oligonucleotide comprises an extended oligonucleotide.

58. The method of Claim 56, wherein said reactant is a ligase, and said modified oligonucleotide comprises a ligated oligonucleotide.

59. The method of Claim 56, wherein said bridging oligonucleotide is capable of binding to fewer than ten nucleotides of each of said first and second non-contiguous single-stranded regions.

60. The method of Claim 59, wherein said bridging oligonucleotide is capable of binding to seven or fewer nucleotides of each of said first and second non-contiguous single-stranded regions.

61. The method of Claim 56, wherein said target nucleic acid is DNA.

62. The method of Claim 61, wherein said DNA is viral DNA.

63. The method of Claim 62, wherein said virus is selected from the group consisting of *Parvoviridae, Papovaviridae, Adenoviridae, Hepadnaviridae, Herpesviridae, Iridoviridae,* and *Poxviridae.*

64. The method of Claim 56, wherein said target nucleic acid is RNA.

65. The method of Claim 64, wherein said RNA is viral RNA.

66. The method of Claim 65, wherein said virus is selected from the group consisting of *Picornaviridae, Caliciviridae, Reoviridae, Togaviridae, Flaviviridae, Orthomyxoviridae, Paramyxoviridae, Arenaviridae, Rhabdoviridae, Coronaviridae, Bunyaviridae,* and *Retroviridae.*

67. A method, comprising:

a) providing:

i) target nucleic acid comprising first and second non-contiguous single-stranded regions separated by an intervening region comprising a double-stranded region;

ii) a bridging oligonucleotide capable of binding to said first and second non-contiguous single-stranded regions;

iii) a second oligonucleotide capable of binding to a portion of said first non-contiguous single-stranded region; and

iii) a cleavage means;

b) mixing said target nucleic acid, said bridging oligonucleotide, said second oligonucleotide, and said cleavage means under conditions such that either said second oligonucleotide or said bridging oligonucleotide is cleaved.

68. The method of Claim 67, wherein said cleavage means comprises a nuclease.

69. The method of Claim 68, wherein said cleavage means comprises a thermostable 5' nuclease.

70. The method of Claim 69, wherein said thermostable 5' nuclease comprises an altered polymerase derived from a native polymerases of *Thermus* species.

71. The method of Claim 68, wherein said nuclease is selected from the group consisting of *Pyrococcus woesii* FEN-1 endonuclease, *Methanococcus jannaschii* FEN-1 endonuclease, *Pyrococcus furiosus* FEN-1 endonuclease, and *Archaeoglobus fulgidus* FEN-1 endonuclease.

72. The method of Claim 67, wherein said conditions of said mixing allow for hybridization of said bridging oligonucleotide and said second oligonucleotide to said target nucleic acid so as to define a region of overlap of said oligonucleotides.

73. The method of Claim 72, wherein said region of overlap comprises one base.

74. The method of Claim 72, wherein said region of overlap comprises more than one base.

75. The method of Claim 67, wherein said target nucleic acid is DNA.

76. The method of Claim 75, wherein said DNA is viral DNA.

77. The method of Claim 76, wherein said virus is selected from the group consisting of *Parvoviridae, Papovaviridae, Adenoviridae, Hepadnaviridae, Herpesviridae, Iridoviridae,* and *Poxviridae.*

78. The method of Claim 67, wherein said target nucleic acid is RNA.

79. The method of Claim 78, wherein said RNA is viral RNA.

80. The method of Claim 79, wherein said virus is selected from the group consisting of *Picornaviridae, Caliciviridae, Reoviridae, Togaviridae, Flaviviridae, Orthomyxoviridae, Paramyxoviridae, Arenaviridae, Rhabdoviridae, Coronaviridae, Bunyaviridae,* and *Retroviridae.*

81. A method, comprising:

a) providing:

i) target nucleic acid comprising first and second non-contiguous single-stranded regions separated by an intervening region, said intervening region comprising a first double-stranded portion and a second double-stranded portion separated by a connecting single-stranded portion; and

ii) a bridging oligonucleotide capable of binding to said first and second non-contiguous single-stranded regions; and

b) mixing said target nucleic acid and said bridging oligonucleotide under conditions such that said bridging oligonucleotide hybridizes to said target to form an oligonucleotide/target complex.

82. The method of Claim 81, wherein said target nucleic acid is DNA .

83. The method of Claim 82, wherein said DNA is viral DNA.

84. The method of Claim 83, wherein said virus is selected from the group consisting of *Parvoviridae, Papovaviridae, Adenoviridae, Hepadnaviridae, Herpesviridae, Iridoviridae,* and *Poxviridae.*

85. The method of Claim 81, wherein said target nucleic acid is RNA.

86. The method of Claim 85, wherein said RNA is viral RNA.

87. The method of Claim 86, wherein said virus is selected from the group consisting of *Picornaviridae, Caliciviridae, Reoviridae, Togaviridae, Flaviviridae, Orthomyxoviridae, Paramyxoviridae, Arenaviridae, Rhabdoviridae, Coronaviridae, Bunyaviridae,* and *Retroviridae.*

88. A method for the analysis of nucleic acid structures comprising;

a) providing:

i) a sequence data input means;

ii) a cleavage data input means; and

iii) a nucleic acid structure prediction means;

b) providing nucleic acid sequence data to said sequence data input means to produce sequence data results;

c) providing structure-specific cleavage data to said cleavage data input means to produce cleavage data results; and

d) providing said sequence data results and said cleavage data results to said nucleic acid structure prediction means to produce a predicted nucleic acid structure.

89. The method of Claim 87, futher comprising the steps of e) providing a basepair data input means and a second nucleic acid structure prediction means; f) providing basepair data to said basepair data input means to produce basepair data results; and g) providing said sequence data results, said cleavage data results, and said basepair data results to said second nucleic acid structure prediction means to produce a second predicted nucleic acid structure.